

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-45 (Canceled)

46. (Currently amended) A method for preparing a ~~stable liposome vesicle-entrapped chemical species~~ pharmaceutical preparation for administration *in vivo* to an animal, which comprises the steps of:

- (a) forming liposomes ~~comprising a membrane~~ in:
 - (1) an aqueous medium containing an acid which is substantially impermeable through the vesicle to give an acidic liposome-containing aqueous medium in which the acid is present in the internal and external liposome phases; or
 - (2) an aqueous medium containing a base which is substantially impermeable through the vesicle to give ~~an~~ a basic liposome-containing aqueous medium in which the base is present in the internal and external liposome phases;
- (b) adding:

- (1) to the thus-obtained ~~acid~~ acidic liposome-containing aqueous medium a permanently charged, chargeable, or pH titratable ~~chemical-species~~ drug which is a cationic ~~chemical-species~~, or
 - (2) to the thus-obtained ~~acid~~ basic liposome-containing aqueous medium a permanently charged, chargeable, or pH titratable ~~chemical-species~~ drug which is an anionic ~~chemical-species~~; and
- (c) adding to the external liposome phase:
- (1) a base to ~~provide a pH gradient across the membrane of the liposome and~~ thereby induce the cationic ~~chemical-species~~ drug to pass into the liposomes' internal acidic aqueous phase, or
 - (2) an acid to ~~provide a pH gradient across the membrane of the liposome and~~ thereby induce the anionic ~~chemical-species~~ drug to pass into the liposomes' internal basic aqueous phase;

wherein said cationic ~~chemical-species~~ drug or said anionic ~~chemical-species~~ drug is accumulated and entrapped within said liposome to produce a stable liposome vesicle-entrapped ~~chemical-species~~ drug; and

(d) suspending the vesicles for administration in a bulk solution, wherein the bulk solution has a pH which is physiologically benign.

~~, said stability being independent of maintenance of a pH gradient across the liposome membrane after entrapment of the chemical species such that after administration to an animal the chemical species is carried to its destination by the liposome vesicle before significant leakage occurs, and the animal suffers no long term effects of the administration.~~

47. (Canceled)

48. (Previously presented) The method according to Claim 46 wherein the aqueous medium is a buffer solution.

49. (Currently amended) A ~~liposome-vesicle-entrapped chemical species~~ pharmaceutical preparation for administration in vivo to an animal prepared by the method of Claim 46.

50. (Canceled)

51. (Canceled)

52. (Currently amended) A method of preparing a ~~stable liposome-vesicle-entrapped chemical species~~ pharmaceutical preparation for administration in vivo to an animal, which method comprises:

- (a) forming liposomes in:
 - (1) an aqueous medium containing an acid which is substantially impermeable through the vesicle to give an acidic liposome-containing aqueous medium in which the acid is present in the internal and external liposome phases; or

- (2) an aqueous medium containing a base which is substantially impermeable through the vesicle to give an basic liposome-containing aqueous medium in which the base is present in the internal and external liposome phases;
- (b) adding:
 - (1) to the thus-obtained acid liposome-containing aqueous medium a permanently charged, chargeable, or pH titratable ~~chemical species~~ drug which is a cationic ~~chemical species~~, or
 - (2) to the thus-obtained acid liposome-containing aqueous medium a permanently charged, chargeable, or pH titratable ~~chemical species~~ drug which is an anionic ~~chemical species~~; and
- (c) adding to the external liposome phase:
 - (1) a base in an amount effective to create a pH gradient between the external liposome phase and the internal liposome phase to thereby induce the cationic ~~chemical species~~ drug to pass into the liposomes' internal acidic aqueous phase, or
 - (2) an acid in an amount effective to create a pH gradient between the external liposome phase and the internal liposome phase to thereby induce the anionic ~~chemical species~~ drug to pass into the liposomes' internal basic aqueous phase;

wherein said cationic ~~chemical species~~ drug or said anionic ~~chemical species~~ drug is accumulated and entrapped within said liposome to produce a stable liposome

vesicle-entrapped ~~chemical-species drug~~, said stability being independent of maintenance of the pH gradient after entrapment of the ~~chemical-species drug~~ such that after administration to an animal the ~~chemical-species drug~~ is carried to its destination by the liposome vesicle before significant leakage occurs, and the animal suffers no long-term effects of the administration.

53. (Canceled)

54. (Currently amended) The method of Claim 52, wherein the ~~charged-chemical species is a drug having~~ has hydrophobic ions.

55. (Previously presented) The method of Claim 54, wherein the drug having hydrophobic ions is ellipticinium chloride, an antihelminthic, gentian violet, pyrvinium, pamoate, a cyanine dye, or pamaguine.

56. (Previously presented) The method of Claim 53, wherein the drug is a drug for chemotherapy or immunosuppression, a membrane permeable peptide toxin or a hormone.

57. (Currently amended) The method of Claim 52, wherein the pH titratable ~~chemical-species is a drug having molecules with~~ has basic properties.

58. (Previously presented) The method of Claim 57, wherein the drug is vincristine, doxorubicin, streptomycin, chloroquine, daunorubicin.

59. (Currently amended) The method of Claim 52, wherein the pH titratable ~~chemical species is a drug having molecules with~~ has acidic properties.

60. (Previously presented) The method of Claim 59, wherein the drug is a derivative of methotrexate, daunomycin, penicillin or a salicylic acid derivative.

61. (Previously presented) The method according to Claim 52 wherein the aqueous medium is a buffer solution.

62. (Currently amended) A ~~liposome vesicle entrapped chemical species~~ pharmaceutical preparation for administration in vivo to an animal prepared by the method of Claim 52.

63. (Canceled)

64. (Canceled)

65. (Previously presented) The method of Claim 60, wherein said salicylic acid derivative is p-amino salicylic acid.